

What is claimed is:

1. A method for reducing the immunostimulatory effect of a CpG-containing oligonucleotide, the method comprising introducing a 3' substituted nucleoside into the oligonucleotide at a position adjacent to, and on the 5' side of the CpG dinucleotide.
2. The method according to claim 1, wherein the method is used to make an oligonucleotide that is complementary to a gene or gene transcript.
3. The method according to claim 2, wherein the oligonucleotide has antisense activity.
4. The method according to claim 1, wherein only one 3' substituted nucleoside is introduced into the oligonucleotide for each CpG dinucleotide present in the oligonucleotide.
5. The method according to claim 1, wherein only one 3' substituted nucleoside is introduced into the oligonucleotide.
6. A CpG-containing oligonucleotide having a reduced immunostimulatory effect, wherein the oligonucleotide comprises a 3' substituted nucleoside at a position adjacent to, and on the 5' side of the CpG dinucleotide.
7. The oligonucleotide according to claim 6, wherein the oligonucleotide is from about 12 to about 50 nucleotides in length.

8. The oligonucleotide according to claim 7, wherein the oligonucleotide is from about 17 to about 35 nucleotides in length.
9. The oligonucleotide according to claim 6, wherein oligonucleotide is complementary to a gene or gene transcript.
10. The oligonucleotide according to claim 9, wherein oligonucleotide has antisense activity.
11. The oligonucleotide according to claim 6, wherein the oligonucleotide has only one 3' substituted nucleoside for each CpG dinucleotide present in the oligonucleotide.
12. The oligonucleotide according to claim 6, wherein the oligonucleotide has only one 3' substituted nucleoside.
13. A method for obtaining an antisense-specific reduction in the expression of a gene in a mammal, the method comprising administering to the mammal a CpG-containing oligonucleotide having a reduced immunostimulatory effect, wherein the oligonucleotide comprises a 3' substituted nucleoside at a position adjacent to, and on the 5' side of the CpG dinucleotide.
14. The method according to claim 13, wherein the oligonucleotide has only one 3' substituted nucleoside for each CpG dinucleotide present in the oligonucleotide.
15. The method according to claim 13, wherein the oligonucleotide has only one 3' substituted nucleoside.

16. A method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide, the method comprising introducing into the oligonucleotide a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

17. The method according to claim 16, wherein the oligonucleotide is not an antisense oligonucleotide.

18. A CpG-containing oligonucleotide having increased immunostimulatory effects, the oligonucleotide comprising a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

19. The oligonucleotide according to claim 18, wherein the oligonucleotide is not an antisense oligonucleotide.

20. The oligonucleotide according to claim 18, wherein the oligonucleotide is from about 6 to about 50 nucleotides in length.

21. The oligonucleotide according to claim 18, wherein the oligonucleotide further comprise modified internucleotide linkages or modified sugars to improve stability.

22. A method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

23. The method according to claim 22, wherein the oligonucleotide is not an antisense oligonucleotide.

24. A method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide, the method comprising introducing into the oligonucleotide an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the

CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

25. The method according to claim 24, wherein the uncharged internucleoside linkage is an alkylphosphonate.

26. The method according to claim 25, wherein the alkylphosphonate is a methylphosphonate.

27. The method according to claim 24, wherein the oligonucleotide is not an antisense oligonucleotide.

28. A CpG-containing oligonucleotide having increased immunostimulatory effects, the oligonucleotide comprising an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

29. The oligonucleotide according to claim 28, wherein the uncharged internucleoside linkage is an alkylphosphonate.

30. The oligonucleotide according to claim 29, wherein the alkylphosphonate is a methylphosphonate.

31. The oligonucleotide according to claim 28, wherein the oligonucleotide is not an antisense oligonucleotide.

32. The oligonucleotide according to claim 28, wherein the oligonucleotide is from about 6 to about 50 nucleotides in length.

33. The oligonucleotide according to claim 28, wherein the oligonucleotide further comprise modified internucleotide linkages or modified sugars to improve stability.

34. A method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

35. The method according to claim 34, wherein the uncharged internucleoside linkage is an alkylphosphonate.

36. The method according to claim 35, wherein the alkylphosphonate is a methylphosphonate.

37. The method according to claim 34, wherein the oligonucleotide is not an antisense oligonucleotide.

38. A method for reducing the immunostimulatory effect of a CpG-containing oligonucleotide, the method comprising introducing a 2'-5' internucleoside linkage into the oligonucleotide at a position adjacent to, and on the 5' side of the CpG dinucleotide.

39. The method according to claim 38, wherein the method is used to make an oligonucleotide that is complementary to a gene or gene transcript.

40. The method according to claim 39, wherein the oligonucleotide has antisense activity.

41. The method according to claim 38, wherein only one 2'-5' internucleoside linkage is introduced into the oligonucleotide for each CpG dinucleotide present in the oligonucleotide.

42. The method according to claim 38, wherein only one 2'-5' internucleoside linkage is introduced into the oligonucleotide.

43. A CpG-containing oligonucleotide having a reduced immunostimulatory effect, wherein the oligonucleotide comprises a 2'-5' internucleoside linkage at a position adjacent to, and on the 5' side of the CpG dinucleotide.

44. The oligonucleotide according to claim 43, wherein the oligonucleotide is from about 12 to about 50 nucleotides in length.

45. The oligonucleotide according to claim 44, wherein the oligonucleotide is from about 17 to about 35 nucleotides in length.

46. The oligonucleotide according to claim 43, wherein oligonucleotide is complementary to a gene or gene transcript.

47. The oligonucleotide according to claim 46, wherein oligonucleotide has antisense activity.

48. The oligonucleotide according to claim 43, wherein the oligonucleotide has only one 2'-5' internucleoside linkage for each CpG dinucleotide present in the oligonucleotide.

49. The oligonucleotide according to claim 43, wherein the oligonucleotide has only one 3' substituted nucleoside.

50. A method for obtaining an antisense-specific reduction in the expression of a gene in a mammal, the method comprising administering to the mammal a CpG-containing oligonucleotide having a reduced immunostimulatory effect, wherein the oligonucleotide comprises a 2'-5' internucleoside linkage at a position adjacent to, and on the 5' side of the CpG dinucleotide.

51. The method according to claim 50, wherein the oligonucleotide has only one 2'-5' internucleoside linkage for each CpG dinucleotide present in the oligonucleotide.

52. The method according to claim 50, wherein the oligonucleotide has only one 2'-5' internucleoside linkage.



53. A method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide, the method comprising introducing into the oligonucleotide a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

54. The method according to claim 53, wherein the 2'-5' internucleoside linkage is an alkylphosphonate.

55. A CpG-containing oligonucleotide having increased immunostimulatory effects, the oligonucleotide comprising a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

56. The oligonucleotide according to claim 55, wherein the oligonucleotide is not an antisense oligonucleotide.

57. The oligonucleotide according to claim 55, wherein the oligonucleotide is from about 6 to about 50 nucleotides in length.

58. The oligonucleotide according to claim 55, wherein the oligonucleotide further comprise modified internucleotide linkages or modified sugars to improve stability.

59. A method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2 nucleosides 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, and combinations thereof.

60. The method according to claim 59, wherein the oligonucleotide is not an antisense oligonucleotide.